Applicants submit that they have re-checked the amendments made on December 5, 2001 and they correspond to the cited pages of Applicant's copy of the specification. Applicant's request additional clarification from the Examiner as to where, specifically, the lack of correspondence occurs.

Rejection of claims 7-14, 24-24, and 26-28 under 35 U.S.C. §101

The Examiner has rejected claims 7-14, 23, 24, and 26-28 under 35 U.S.C. §101 for lack of utility. The Examiner asserts that the invention is not supported by either a well established utility or a specific, substantial, and credible utility. Applicants respectfully disagree.

The Examiner asserts that because the specification does not disclose the precise biological function of GPR86, one of skill in the art would not be able to recognize the specific and substantial use of GPR86, or the claimed methods of screening for candidate modulators of GPR86 activity. The Examiner also asserts that although the specification teaches that the invention provides methods of diagnosing a disease or disorder characterized by dysregulation of GPR86 signaling, the utility is not specific and substantial because they do not identify or reasonably confirm a "real world" context of use. Applicants respectfully submit that the Examiner is in error.

The Utility Examination Guidelines (Fed. Reg. 66, 2001, p. 1092) clearly articulate that if the applicant has asserted that the claimed invention is "useful for **any particular practical purpose** (i.e., it has a "specific and substantial utility") and the assertion would be considered credible by a person of ordinary skill in the art, do not impose a rejection based on lack of utility". The guidelines go on to explain the meaning of specific and substantial describing that the requirement excludes "throw away", "insubstantial" or "nonspecific" utilities, "such as the use of a complex invention as landfill". The guidelines indicate that credibility is to be judged from the perspective of one of ordinary skill in the art, and that Applicants need only provide one credible assertion of a specific and substantial utility to meet the requirement.

Applicants submit that the present specification provides a credible assertion of a specific and substantial utility for the invention as claimed. The specification teaches that GPR86 is a G-

protein coupled receptor which acts as a receptor for ADP. The specification teaches further at page 43, lines 18-23 that

> GPR86, which is expressed in cells of the lymphocytic lineages, platelets, spleen as well as leukemic cells, can have a role in immune processes, cancer, thrombosis and associated disorders or diseases. The GPR86 expression pattern also includes the brain and further suggests a potential role as an ADP neurotransmitter. **The expression pattern of GPR86 and the knowledge with respect to disorders generally mediated by GPCRs suggests that GPR86 can be involved in disturbances of**....[the specification then provides a list of target diseases and disorders]

The specification teaches further that the "interaction of GPR86 with ADP can be used as the basis of assays for the diagnosis or monitoring of diseases, disorders, or processes involving GPR86 signaling" (page 44, lines 7-8). Thus, the specification teaches that GPR86 has a characteristic cellular distribution which is indicative of its role in physiological processes which are consistent with the specific cellular distribution taught in the specification.

Applicants submit that GPCRs are well known to those of skill in the art as transmembrane proteins which function to transduce a signal from the outside to the inside of a cell. Applicants submit further, that the use of a protein's tissue or cellular distribution is widely accepted by those of skill in the art for purposes of making deductions as to the physiological role of the protein, and its possible function in a disease state. It is well known to those of skill in the art that the putative function for a protein is often based solely on its distribution in a particular set of tissues. See, for example, Beaudet et al., 1998, *J Neurobiol.* 36:325 [teaching that expression of pituitary adenylate cyclase in a population of sympathetic preganglionic neurons was indicative of the peptide functioning as a preganglionic sympathetic neurotransmitter].

The Examiner seems to be asserting that the only disclosure which would satisfy the utility requirement would be a full characterization of protein physiology, and a complete description of protein function. This is not what is required by the utility guidelines. The specification teaches that GPR86 is a G-protein coupled receptor; it teaches that the natural ligand of GPR86 is ADP, a known signaling molecule and neurotransmitter; it teaches that the receptor is expressed in lymphocytic cells, platelets, spleen cells, and the brain, imputing a role

for GPR86 in diverse physiological processes including immune processes, cancer, thrombosis, and neurotransmission. Applicants submit that this description is a specific and substantial assertion of a credible utility for GPR86. The Examiner points out that, as cited in *Brenner v. Manson*, 383 U.S. 519 (Sup. Ct. 1966), "a patent is not a hunting license...it is not a reward for the search, but compensation for its successful conclusion". Applicants concur with this sentiment, however, submit that the present disclosure goes far beyond providing a mere hunting license. Applicants have discovered that ADP, a known signaling molecule, is the natural ligand for the G-protein coupled receptor GPR86, and that the receptor is distributed is specific tissues which is indicative of the receptor, and more importantly, the receptor/ligand interaction having a specific physiological role. In view of the specific and substantial disclosure provided in the specification, the Examiner has not provided a rationale as to why one of skill in the art would not find such an asserted use to be credible. Applicants submit that given the teachings in the specification, one of skill in the art would readily appreciate and concur with the asserted usefulness of the present invention.

Applicants accordingly submit that the present invention is supported by a substantial, specific, and credible utility, and therefore request that the rejection be reconsidered and withdrawn.

Rejection of claims 7-14, 23, 24, and 26-28 under 35 U.S.C. §112, second paragraph

The Examiner has rejected claims 7-14, 23, 24, and 26-28 under 35 U.S.C. §112, second paragraph as being indefinite on several grounds.

The Examiner asserts that the claims are indefinite because they recite the term GPR86; the Examiner asserts that GPR86 should be set forth by its SEQ ID NO. Applicants respectfully disagree.

Applicants submit that by their amendment of December 5, 2001, the amino acid sequence of GPR86 was indicated to be set forth in SEQ ID NO: 2. While the rules governing the disclosure of sequences in a patent application require that "where the description or claim of a patent application **discuss a sequence** that is set for the in the "Sequence Listing"...reference must be made to the sequence by use of the sequence identifier" (37 C.F.R. §1.821), there is no

requirement that the mere use of the **name** of a sequence must be accompanied by reference to the sequence identifier. To extend the requirement of 37 C.F.R. 1.821 to the extent suggested by the Examiner would mean that each time GPR86 is mentioned in the specification, Applicants would be required to indicate a sequence identifier; clearly, Applicants are not required to do this. The claims of the present invention refer to GPR86. Given the teaching in the specification and figures, one of skill in the art would readily be able to determine the metes and bounds of GPR86.

Applicants submit that the Examiner has not presented any rationale as to why applicants should be required to modify the claims of the present invention, when they are clear and definite as written. If the Examiner contends that one of skill in the art would be confused by, or not comprehend the scope of the recitation of GPR86 in the claims, given the teachings in the specification, Applicants respectfully request that the Examiner provide Applicants with a rationale to support this position.

The Examiner has rejected claims 7-14 and 26-28 as being indefinite in the recitation of "said second messenger assays" because there is no antecedent basis. The Examiner has rejected the claims further for the recitation of "detecting a signaling activity", because it is unclear what signaling activity is to be determined.

With respect to "said second messenger assays", Applicants submit that they have amended the claims to include proper antecedent basis. With respect to the phrase "detecting a signaling activity", Applicants submit that the specification clearly indicates that "the step of measuring a signaling activity of the GPR86 polypeptide comprises detecting a change in the level of a second messenger" (page 5, lines 24-25). Thus, Applicants submit that, from a reading of the specification, it would be clear to one of skill in the art what is meant by "detecting a signaling activity". Nevertheless, in order to advance prosecution, Applicants have amended the claims herein to recite "detecting a signaling activity of GPR86 polypeptide...*by a second messenger assay*".

The Examiner has rejected claims 8 and 12 as being indefinite in the recitation of "other cell lines". Applicants submit that the phrase "other cell lines" has been deleted from these claims.

The Examiner has rejected claims 7, 9, 11, 13, and 23 as being indefinite for failing to recite a correlation step linking the detection/selection steps to the goal recited in the preamble. Applicants submit that the claims have been amended to recite an appropriate correlation step.

Applicants submit that the claims are definite as amended, and therefore request that the rejections be reconsidered and withdrawn.

Conclusion

Applicants submit that in view of the foregoing remarks, all issues relevant to patentability raised in the Office Action have been addressed. Applicants respectfully request the withdrawal of rejections over the claims of the present invention.

Respectfully submitted,

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MARKED-UP VERSION OF AMENDMENTS:

Claim Amendments Under 37 C.F.R. § 1.121(c)(1)(ii)

7. (Amended) A method of screening for a candidate modulator of GPR86 activity using cells expressing GPR86, said method compromising:

a) incubating a first sample of said cells in the presence of said candidate modulator and a second sample of said cells in the absence of said candidate modulator, both said samples under conditions which permit binding of ADP to GPR86;

b) detecting a signalling activity of GPR86 polypeptide in said first and second samples by a second messenger assay, and

c) comparing the results of said second messenger assays for said first and second samples, wherein a difference in activity between said first and second samples is indicative of said candidate modulator being a modulator of GPR86 activity.

8. (Amended) The method of claim 7 wherein said cell is selected from the group consisting of: COS7-cells, a CHO cell, a LM (TK-) cell, a NIH-3T3 cell, HEK-293 cell, K-562 cell, a 1321N1 astrocytoma cell [and other cell lines].

9. (Amended) A method of screening for a candidate modulator of GPR86 activity using cell membranes bearing GPR86, said method comprising:

a) incubating a first sample of said cell membranes in the presence of said candidate modulator and a second sample of said cell membranes in the absence of said candidate modulator, both said samples under conditions which permit binding of ADP to GPR86;

b) detecting a signalling activity of GPR86 polypeptide in said first and second samples by a second messenger assay, and

c) comparing the results of said second messenger assays for said first and second samples, wherein a difference in activity between said first and second samples is indicative of said candidate modulator being a modulator of GPR86 activity.

11. (Amended) A method for determining if a candidate modulator increases or decreases the activity of GPR86 using cells expressing GPR86, said method comprising:

a) incubating a first sample of said cells in the presence of said candidate modulator and a second sample of said cells in the absence of said candidate modulator, both said samples under conditions which permit binding of ADP to GPR86;

b) detecting a signalling activity of GPR86 polypeptide in said first and second samples by a second messenger assay, and

c) comparing the results of said second messenger assays for said first and second samples, wherein a difference in activity between said first and second samples is indicative of said candidate modulator as increasing or decreasing GPR86 activity.

12. (Amended) The method of claim 11 wherein said cells are selected from the group consisting of: COS7-cells, a CHO cell, a LM (TK-) cell, a NIH-3T3 cell, HEK-293 cell, K-562 cell and a 1321N1 astrocytoma cell [and other cell lines].

13. (Amended) A method for determining if a candidate modulator increases or decreases the activity of GPR86 using cell membranes bearing GPR86, said method comprising:

a) incubating a first sample of said cell membranes in the presence of said candidate modulator and a second sample of said cell membranes in the

absence of said candidate modulator, both said samples under conditions which permit binding of ADP to GPR86;

b) detecting a signalling activity of GPR86 polypeptide in said first and second samples by a second messenger assay, and

c) comparing the results of said second messenger assays for said first and second samples, wherein a difference in activity between said first and second samples is indicative of said candidate modulator increasing or decreasing GPR86 activity.

23. (Amended) A method of identifying an agent that modulates the function of GPR86, said method comprising:

a) contacting a GPR86 polypeptide in the presence and absence of a candidate modulator under conditions permitting the binding of said ADP to said GPR86 polypeptide; and

b) measuring the binding of said GPR86 polypeptide to said candidate modulator, relative to the binding in the absence of said candidate modulator, wherein a difference in binding identifies said candidate modulator as an agent that modulates the function of GPR86.